

## RESEARCH NOTE

### Drug resistance among *Mycobacterium tuberculosis* strains in immigrants: is there a real threat everywhere?

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#### ABSTRACT

A study was performed to determine the impact of drug resistance in tuberculosis among immigrant patients in Madrid, Spain. During the period 1995–2001, the relative proportion of isolates from immigrant patients increased from 4.4% to 24.2%. No differences between immigrants and Spanish-born patients were detected for resistance to any first-line anti-tuberculous drug. More studies are required to determine the actual incidence of resistant tuberculosis in immigrants.

**Keywords** Tuberculosis, drug resistance, immigrants, prevalence

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The importance of globalisation and mass movements of populations in the epidemiology of tuberculosis is a fact that has been recognised previously in many studies [1,2]. One particular aspect that has been a subject of concern is the risk of spread of resistant strains among the population [3]. Recent reports suggest different prophylactic regimens for patients according to their country of origin [4]. Spain is of special interest because it is

between the European Union and Northern Africa, and is also the destination of many immigrants from Central and South America. This Research Note compares resistance data for immigrants in Madrid with data for Spanish-born people in the period 1995–2001.

During the study period, 457 consecutive patients were diagnosed with tuberculosis by culture. Among these, 69 were immigrants from different geographical areas (Ecuador and Morocco, 16 cases each; Peru, six cases; Colombia, five cases; Portugal, four cases; and other countries from South America, Africa and Asia, all with less than three cases each). The relative percentage of isolates from immigrants with tuberculosis grew from 4.4% in 1995 to 24.2% in 2001 ( $p < 0.01$ ,  $\chi^2$  for trends).

All samples in the study period were processed according to commonly accepted protocols, and all the isolates were sent to the Centro Nacional de Microbiología (Majadahonda, Spain) to confirm the identification and susceptibility testing results. The isolates were identified as *Mycobacterium tuberculosis* in 440 cases, *M. bovis* in 13 cases, and *M. africanum* in four cases. All *M. bovis* isolates were from Spanish-born patients, and all *M. africanum* isolates were from immigrant patients.

Resistance to at least one of the first-line anti-tuberculous drugs was detected in four (5.8%) isolates among immigrants, and in 28 (6.7%) isolates among Spanish-born patients. These data could be influenced by the isolation of several multidrug-resistant *M. bovis* strains from unrelated patients that were related temporally to strains from several outbreaks reported previously. When only *M. tuberculosis* isolates from immigrant and Spanish-born patients were compared for drug resistance, no statistically significant differences were detected for any of the antimicrobial agents included in the study (Fisher's exact test; Table 1), although a slight increase in the resistance rates among immigrant patients was observed. Only two immigrants (both from South America) showed multidrug-resistant tuberculosis, and in both cases the resistance was secondary to inadequate therapies. No resistant strains were isolated from African patients.

The importance of migration in the epidemiology of tuberculosis in developed countries has recently been of increasing interest [5–8]. In

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**Table 1.** Resistance rates of *Mycobacterium tuberculosis* among immigrants and Spanish-born patients

| Antibiotic   | Spanish-born<br>( <i>n</i> = 406)<br>% resistance ( <i>n</i> ) | Immigrants<br>( <i>n</i> = 65)<br>% resistance ( <i>n</i> ) | <i>p</i> |
|--------------|--|---|----------|
| Isoniazid    | 3.0% (12)  | 4.7% (3)  | 0.471    |
| Rifampicin   | 1.5% (6)   | 3.1% (2)  | 0.333    |
| Streptomycin | 1.2% (5)   | 3.1% (2)  | 0.274    |
| Ethambutol   | 0.5% (2)   | 1.6% (1)  | 0.380    |
| Pyrazinamide | 0.5% (2)   | 3.1% (2)  | 0.117    |

several reports, tuberculosis in this population represented a significant proportion of the total cases recognised, and even the majority of cases in some countries [8,9]. The knowledge that resistance rates in some of the origin countries are higher than in the destination countries [3,10,11], and that the risk of transmission exists, albeit at a low frequency, between immigrants and local populations [12], highlights the risk of introduction of drug-resistant strains into countries which currently have a low incidence of such strains. In many studies, immigrant patients had higher rates of resistance than native patients [7,13–15], but contrasting data have been obtained in other studies [16]. According to the data in the present study, tuberculosis in immigrants in Madrid shows similar resistance rates to those found in Spanish-born patients, and even multidrug-resistant strains were not the result of primary resistance, but secondary to inadequate therapy. Perhaps differences in the immigrant populations could explain the differences between the various studies. The relatively low number of cases in the present study is an important limitation, especially when other studies in Spain have yielded different results [6,14]. A large study is needed to establish the actual resistance rates in native and immigrant populations. Until such data are available, treatment with four drugs, coupled with a proper history of previous therapies and the performance of cultures and antibiograms, must be regarded as necessary practice for the management of immigrant patients.

## REFERENCES

1. Hamburg MA, Frieden TR. Tuberculosis transmission in the 1990s. *N Engl J Med* 1994; **330**: 1750–1751.
2. Raviglione MC, Snider DE, Kochi A. Global epidemiology of tuberculosis: Morbidity and mortality of a worldwide epidemic. *JAMA* 1995; **273**: 220–226.
3. Espinal MA, Laszlo A, Simonsen L *et al.* Global trends in resistance to antituberculosis drugs. World Health Organization-International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. *N Engl J Med* 2001; **344**: 1294–1303.
4. Khan K, Muennig P, Behta M, Zivin JG. Global drug-resistance patterns and the management of latent tuberculosis infection in immigrants to the United States. *N Engl J Med* 2002; **347**: 1850–1859.
5. Rieder HL, Zellweger JP, Raviglione MC, Keizer ST, Migliori GB. Tuberculosis control in Europe and international migration. *Eur Resp J* 1994; **7**: 1545–1553.
6. Valles X, Sanchez F, Panella H *et al.* [Imported tuberculosis: an emerging disease in industrialised countries]. *Med Clínica (Barcelona)* 2002; **118**: 376–378.
7. Sánchez-Gascón F, Bernabeu-Mora R. Inmigración y tuberculosis. *Arch Bronconeumologia* 2003; **39**: 5–7.
8. De March-Ayuela P. Tuberculosis importada. Cuál es la tuberculosis autóctona española? *Med Clínica (Barcelona)* 2002; **119**: 677.
9. Laserson KF, Iademarco MF. Profiling drug resistance in immigrants with tuberculosis. *Chest* 2000; **117**: 623–625.
10. Mertz BL, Douce RW, Brito N. Anti-tuberculosis drug resistance in two clinics in Ecuador. *Int J Tuberc Lung Dis* 2000; **4**: 115–117.
11. Soualhine H, Benlemlih M, Oudghiri N, El Messaoudi D, Timinouni M. Rapid detection of rifampin-resistance mutations in multidrug-resistant strains of *Mycobacterium tuberculosis* in Morocco. *Eur J Clin Microbiol Infect Dis* 2001; **20**: 596–597.
12. Lillebaek T, Andersen AB, Bauer J *et al.* Risk of *Mycobacterium tuberculosis* transmission in a low-incidence country due to immigration from high-incidence areas. *J Clin Microbiol* 2001; **39**: 855–861.
13. Gilad J, Borer A, Riesenberger K, Peled N, Schaeffler F. Epidemiology and ethnic distribution of multidrug-resistant tuberculosis in southern Israel, 1992–97. *Chest* 2000; **117**: 738–743.
14. Hueraga H, Lopez Velez R, Navas E, Gomez Mampaso E. Clinicoepidemiological features of immigrants with tuberculosis living in Madrid, Spain. *Eur J Clin Microbiol Infect Dis* 2000; **19**: 236–237.
15. Infuso A, Antoine D, Barboza P, Falzon D. Surveillance of anti-tuberculous drug resistance in Europe, 1999. *Euro-surveillance* 2002; **7**: 93–100.
16. Munsiff SS, Bassoff T, Nivin B *et al.* Molecular epidemiology of multidrug-resistant tuberculosis, New York City, 1995–97. *Emerg Infect Dis* 2002; **8**: 1230–1238.